

Review of: "Is creeping abandon of human cancer defences evolutionarily favoured?"

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Review of "Is creeping abandon of human cancer defences evolutionary favored?"

The paper "Is creeping abandon of human cancer defences evolutionary favored?" explores the hypothesis that lowering cancer defenses at old ages in Humans might have been favoured by evolution as a mean to ensure that males do not sire too many offspring, thus reducing the negative consequences of inbreeding within a small group.

Before going into a more detailed review, there is one empirical observation that the authors do not take into account : in Humans, cancer incidence (and, as a result, cancer mortality) increases during adulthood and, at old ages, plateaus or even decreases. This pattern is consistent between populations and between tumors and is unlikely to result from a data bias / a cohort effect / only from differential selection (see a review here: <https://www.nature.com/articles/nrc1715>). One question stems from this : how is the authors' hypothesis congruent with that empirical pattern?

Abstract

- it is implied that lowering cancer defences might help individuals invest more in parental/grandparental care but surviving a tumour is costly and would decrease such investment (in the case where individuals do not die from their tumour)

Context

Major flaw

The authors hypothesis relies on the claim that Humans are bad at avoiding cancer but this is not (entirely) supported by the literature.

1) recent large scale studies show that the lifetime cancer risk in different species differ wildly among taxa with some taxa apparently having a larger risk than Humans (see Boddy et al (2020) <https://doi.org/10.1093/emph/eoaa015>; Vincze et al. (2022) <https://doi.org/10.1038/s41586-021-04224-5>; Compton et al. (preprint – 2023) [10.1101/2023.02.15.527881](https://doi.org/10.1101/2023.02.15.527881); Bulls et al. (preprint – 2023) <https://doi.org/10.1101/2022.07.12.499088>)

This literature should be cited if the authors write about "all observed other species", even if they focus on primates/apes later on.

2) the authors cite a paper to claim that Chimpanzees have a lower lifetime risk of getting cancer. The first sentence of

that paper's conclusion is "Considering all available evidence, it is not possible to definitively conclude that humans as a species are at higher risk of developing carcinomas, compared with our closest evolutionary relatives."

I have not found more recent studies to assess their claim.

Minor flaws

- Could the authors provide a reference for the 38%?
- Could the authors define "lifetime cancer risk" more precisely because it is unclear whether they are referencing cancer mortality, cancer prevalence, cancer incidence...? It does matter when comparing studies on non-human species with studies on Humans as the amount of data and the different metrics sometimes differ (see Bulls et al. For a discussion on how metrics can yield different conclusions)
- the authors cite two studies (reduced apoptotic function and differential tumor suppressor expression) to support their claim but as suggested in other reviews, there would be other explanations for those empirical patterns.
- the antagonistic pleiotropy hypothesis was first proposed by Williams (1957)
- "species development" and "oncogene development" : are the authors speaking about evolution?

Setting the hypothesis

Not being either a paleo-anthropologist or a cultural anthropologist, I only have minor comments. Having worked in an anthropology lab, I would suggest that the authors collaborate with paleo/anthropologists as this section lacks references.

- gendered labour in early group of Homo sapiens is highly debated. Please provide references for the fact that only men hunted in those groups.
- the authors seem to be confusing patriarchy/patrilineality/patrilocality (or their female equivalent). Patriarchy is probably not a relevant concept (Collins definition : "society, family, or system is one in which the men have all or most of the power and importance.")) and the two other ideas are discussed here <https://hraf.yale.edu/ehc/summaries/residence-and-kinship#kinship-terminology>.

The diversity of kinship and residence patterns observed across current populations does not confirm or infirm their claim that ancestral populations correspond to their description

- the reference 17 made me question whether the authors were serious about this paper.
- what does "lowering tumour suppression activities as part of a state of ageing" mean?
- as pointed out elsewhere, the reasoning on infection might be simplistic : old individuals exhibit immune senescence that would make them more susceptible to other infections.
- the lower appetite of old people (please provide reference) could be explained by several other facts (for instance, if old

people have less physical activity, their energetic demand would be lower)

- *“Now if epigenetic deactivation of tumour suppressor genes as part of the telomere-triggered senescence process is coded on a dominant gene, then individuals within a tribe would not have been able to betray a tribe-wide lowering of tumour suppression activities, because the men of a tribe do in our setting all carry that gene, and it would remain active when combined with the genes of women entering the tribe from outside.”*

This sentence is not clear and the authors should make it clearer that this is another assumption of their model (along with the social structure assumption and the group-selection assumption).

The hypothesis

- can the authors explain how answering their question will help cancer prevention?

- chimpanzees do not live in patriarchal groups (see, for instance, <https://royalsocietypublishing.org/doi/10.1098/rsos.220904> where the description of fusion-fission shows that Chimps groups also have complex, diverse and dynamic settings + the fact that non-kin associations are also frequent)

Suggested experiments

Other reviews will be more relevant than mine (especially if geneticists or population geneticists are involved)

One comment about the model and taking inspiration from anthropological literature : there is a large body of anthropological literature that explains why modern hunter-gatherer/pastoral groups are not a snapshot of ancestral cavemen (starting with : all modern Human populations are equally evolved) and therefore why the inferences one can made about ancestral populations from those groups are limited.

Overall

The hypothesis that lowering cancer defences could be an adaptation is an interesting one. But the authors build a conceptual framework on claims that are not supported by the literature.

Qeios apparently offers a platform where this paper will benefit from the expertise that is currently lacking a bit. The authors should collaborate with evolutionary biologists, paleo/anthropologists and (population) geneticists to ensure their paper is robust.